CLINICAL VIGNETTE

Daylight Photodynamic Therapy with 5-Aminolevulinic Acid for Actinic Keratoses

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Abstract

Photodynamic therapy uses a photo-activated chemical with a light source to treat large areas of actinic damage. Multiple studies have demonstrated that using daylight as a light source is as effective as conventional blue light photodynamic therapy for low-grade actinic keratoses. Nearly all studies of daylight photodynamic therapy have utilized methyl aminolevulinate, which has limited use in the United States, where aminolevulinic acid remains the agent of choice. Efficacy of aminolevulinic acid in conventional photodynamic therapy is well established, but data for use with daylight photodynamic therapy is limited.

Our single institution retrospective chart review identified seven male patients treated with daylight photodynamic therapy using aminolevulinic acid. All patients underwent incubation of aminolevulinic acid for one hour, followed by direct or indirect sun exposure for two hours.

All patients tolerated the procedure well with minimal pain and crusting. Patients all saw improvements in the degree of actinic damage and actinic keratoses per observations of the treating dermatologist. After a single treatment, all patients developed further actinic keratoses necessitating additional treatment.

In our experience, daylight photodynamic therapy utilizing aminolevulinic acid is a cost-effective and well-tolerated treatment for patients with diffuse actinic keratoses, especially in sensitive areas such as the face and neck.

Introduction

Actinic keratoses (AKs) are common cutaneous pre-cancerous lesions that result from the atypical proliferation of epidermal skin cells. Due to their chronicity and potential for malignant transformation, AKs necessitate a simple and effective treatment.[1,2] Risk factors for AKs include fair skin, older age and male gender.[3] Actinic keratoses can be treated in a variety of ways.[3] Lesion-directed therapies include cryosurgery, laser therapy and curettage.[3] Field-directed therapies include imiquimod, 5-fluorouracil, diclofenac gel, ingenol, and photodynamic therapy (PDT).[3] Photodynamic therapy is an appealing option for the treatment of AKs as large surface areas can be treated relatively quickly with high rates of response and superior cosmetic outcomes.[4]

Photodynamic therapy is based on the principle of activating light sensitive molecules in areas of diseased tissue to create reactive oxygen species, which cause tissue injury and cell death.[1] Conventional PDT involves the topical application and incubation of either 5-aminolevulinic acid (ALA) or its ester methyl aminolevulinate (MAL), which are endogenously converted via the heme biosynthetic pathway to protoporphyrin IX (PpIX) and other photosensitive porphyrin molecules.[1,4-6] These photoactive molecules are then activated by either blue or red spectrum light, and cause selective death of the cells in AKs.[5] A wide range of light sources can be used with PDT, including lasers, filtered xenon arc, metal halide or fluorescent lamps and light emitting diodes (LED). However, the red and blue light that activates PpIX and other porphyrin molecules is included within the spectrum of visible light and, thus, thought to be more effective.[5,6]

Although conventional PDT utilizes artificial light sources for treatment, multiple studies have shown the efficacy of daylight PDT.[2,4,5,7-9] These studies have consistently shown that daylight PDT with MAL cream is as effective as conventional PDT for grade I and II AKs, and is often less painful with fewer skin reactions occurring.[9] While daylight PDT with MAL has been well studied, we are aware of only one case series for daylight PDT using ALA, with treatment extended over a two-day period.[10] Unfortunately, MAL access is limited in the United States, where ALA remains the agent of choice. The efficacy of ALA with conventional PDT has been well established, dating back to a study by Szeimies et al., which showed PDT with ALA to be effective in treating AKs particularly on the face and scalp.[11] Here we present a single institution case-series of seven patients treated with daylight PDT using ALA.

Methods

A retrospective chart review was performed to identify patients treated with daylight PDT utilizing ALA between January 2016 and February 2018. Given that the primary intent of this project was to improve and standardize care at UCLA, this study was granted an exemption for institutional research board approval.

Seven patients were identified, who received a total of nine treatments. All of the patients were male, and all had extensive AKs and actinic damage on the scalp and face (Table 1).

Prior to application, areas were cleaned with either isopropyl or acetone. Aminolevulinic acid was applied to the entire treatment area, with the goal to treat the AKs and the background actinic damage. The ALA was incubated for 1 to 1.5 hours. Most patients (patients 1-6) were instructed to spend two hours in the shade before washing off the ALA. Patient 7, who had extensive sun damage, alternatively had chemical sunscreen applied and then spent two-hours outside in direct sun light. Chemical sunscreens do not block blue or red light and are not thought to affect ALA treatment (See Figure 1 for detailed treatment protocol).

Results

All patients tolerated the treatment well. Typical healing time for most patients was three to four days, with all patients experiencing some redness, peeling, and occasional crusting at the site of treatment. For patient 7, the direct sun exposure resulted in crusting and superficial erosions that took ten days to heal fully, without scarring or complications. Pain was generally minimal for treatment done in the shade (indirect sunlight), but direct sunlight resulted in moderate pain. All of the patients saw improvement in the degree of actinic damage and decrease in AKs, per the observation of each treating dermatologist. Of note, in our experience, all of the patients continued to experience further AKs necessitating treatment, most commonly with cryotherapy. Two patients, patients 2 and 7, received repeat daylight PDT.

Discussion

Actinic keratoses are commonly found on the faces and scalps of fair-skinned men with thinning hair. Field cancerization is challenging to treat due to large surface area.[12] Conventional PDT is limited by the need for specialized equipment and the pain associated with treatment. In our experience, ALA with daylight PDT is a viable treatment option, and is able to be completed within a single day. This is a good option for patients in the United States, where MAL is generally unavailable.

Daylight PDT has been shown to have lower pain scores in comparison to conventional PDT, with higher reported patient satisfaction, presenting an attractive option for the sensitive areas of the face and scalp.[2] Furthermore, studies have established that there is no significant difference in result between daylight PDT and conventional PDT, and patients undergoing both have similar side effects.[4] Most patients would benefit from indirect light, such as sitting in the shade, but patients who need a stronger response can be treated with direct sun light, using a chemical sunscreen.

Based on current consensus, daylight PDT is particularly suitable for widespread damage to the face and scalp given the large surface area and sensitivity of the area.[9] Of note, studies have also shown patients with widespread disease, with greater than 15 lesions, utilizing ALA with conventional PDT is more cost effective when compared to diclofenac, 5-fluorouracil, and imiquimod.[13] Daylight PDT further avoids the additional charge for application of the light source.

Conclusion

Our experience has shown that daylight PDT utilizing ALA is a cost-effective treatment option for patients with diffuse disease. Further study is warranted to determine specific efficacy of daylight PDT with ALA in comparison to other treatment modalities.

Figure 1: Treatment Protocol

1. Clean entire treatment area with acetone or rubbing alcohol.
2. Apply ALA to entire treatment area.
3. Incubate patient with applied ALA in the office in a dark room for one to one-and-a-half hours.
4. Instruct patient to receive indirect sunlight (sit in a shaded area outside or sit by a window indoors) for two hours.
5. Instruct patient to wash of ALA, being careful to not get the ALA in the eyes while washing.
6. Remain indoors and avoid direct and indirect sunlight for at least 72 hours. Apply zinc or titanium sunscreen.
7. Keep treated area moisturized to help soothe the skin.

Table 1: Patient Characteristics

Patient	Sex	Age	Location	Number of Treatments	Light Source
1	M	68	Scalp, temples, cheeks, lower lip	1	Indirect
2	M	77	Scalp, temples, forehead	2	Indirect
3	M	63	Face	1	Indirect
4	M	59	Scalp, forehead	1	Indirect
5	M	76	Scalp, temples, forehead	2	Indirect
6	M	67	Scalp	1	Indirect
7	M	69	Forehead, face, lateral neck	2	Direct

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